

**Abstract**

5 A method for engineering and utilizing large DNA vectors to target, via  
homologous recombination, and modify, in any desirable fashion,  
endogenous genes and chromosomal loci in eukaryotic cells. These large  
DNA targeting vectors for eukaryotic cells, termed LTVECs, are derived from  
fragments of cloned genomic DNA larger than those typically used by other  
10 approaches intended to perform homologous targeting in eukaryotic cells.  
Also provided is a rapid and convenient method of detecting eukaryotic cells  
in which the LTVEC has correctly targeted and modified the desired  
endogenous gene(s) or chromosomal locus (loci) as well as the use of these  
cells to generate organisms bearing the genetic modification.

15